

Handwritten initials/signature

Patent Attorney's Docket No. 003300-581

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)
 Thomas Brodin et al.)
 Application No. 09/365,241)
 Filed: July 30, 1999)
 For: IN SITU INDENTIFICATION OF)
 TARGET STRUCTURES E.G. IN VIVO)
 SELECTION METHOD FOR A PHAGE)
 LIBRARY)



Group Art Unit: 1634
 Examiner: Unassigned

**INFORMATION DISCLOSURE STATEMENT
TRANSMITTAL LETTER**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Enclosed is an Information Disclosure Statement and accompanying form PTO-1449 for the above-identified patent application.

- No additional fee for submission of an IDS is required.
- The fee of \$240.00 (126) as set forth in 37 C.F.R. § 1.17(p) is also enclosed.
- A certification under 37 C.F.R. § 1.97(e) is also enclosed.
- A certification under 37 C.F.R. § 1.97(e), a petition requesting consideration of the information disclosure statement, and the petition fee of \$130.00 (122) as set forth in 37 C.F.R. § 1.17(i) are also enclosed.
- Charge \$_____ to Deposit Account No. _____ for the fee due.
- A check in the amount of \$_____ is enclosed for the fee due.

Information Disclosure Statement Transmittal Letter

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The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17 and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

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INFORMATION DISCLOSURE STATEMENT

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Sir:

This application is a continuation of PCT/SE98/00083.

In accordance with the duty of disclosure as set forth in 37 C.F.R. §1.56, Applicants hereby submit the following information in conformance with 37 C.F.R. §§1.97 and 1.98. Applicants provide copies of the International Search Report dated May 25, 1998 and the International Preliminary Examination Report dated June 9, 1999 from the related International Application. Pursuant to 37 C.F.R. §1.98, a copy of each of the following documents is also enclosed:

- (1) "In vivo selection of a lupus phage-display Fv library", W.V. Williams et al., Abstracts from Immunotechnology, Vol. 2, No. 4 (1996) p. 295-296.
- (2) "In vivo selection of a lupus phage-display Fv library", W.V. Williams et al., Dialog, Abstract No. 13438353 (1996).

- (3) International Patent Publication No. WO 94/26787
METHOD FOR GENERATING CELL TYPE SPECIFIC PHAGE ANTIBODY LIBRARIES
Applicant: The Board of Trustees of the Leland Stanford Junior University
Published: 24 November 1994
- (4) "Autoimmune derived combinatorial phage display libraries: methods in construction of and affinity selection for anti-RNA Fabs", Marie T. Marchbank et al., Nucleic Acids Symposium Series, No. 33 (1995) pp. 120-122.
- (5) "High Affinity, Thyroid-Specific Human Autoantibodies Displayed on the Surface of Filamentous Phage Use V Genes Similar to Other Autoantibodies", Stefano Portolano et al., The Journal of Immunology, Vol. 151, No. 5 (September 1, 1993) pp. 2839-2851. [Also discussed at Page 21 of the Specification.]
- (6) "Toward cell-targeting gene therapy vectors: Selection of cell-binding peptides from random peptide-presenting phage libraries", Michael A. Barry et al., Nature Medicine, Vol. 2, No. 3 (March 1996) pp. 299-305.
- (7) "A melanoma-specific V_H antibody cloned from a fusion phage library of a vaccinated melanoma patient", Xiaohong Cai et al., Proc. Natl. Acad. Sci. USA, Vol. 93 (June 1996) pp. 6280-6285.
- (8) International Patent Publication No. WO 94/28424
METHOD FOR SELECTION OF BIOLOGICALLY ACTIVE PEPTIDE SEQUENCES
Applicant: Chron Corporation
Published: 8 December 1994
- (9) International Patent Publication No. WO 92/15679
IMPROVED EPITODE DISPLAYING PHAGE
Applicant: Protein Engineering Corporation
Published: 17 September 1992

- (10) International Patent Publication No. WO 97/22972
METHOD FOR THE SIMULTANEOUS DETECTION OF A THERAPEUTIC TARGET FOR A DISEASE STATE AND ITS NEUTRALIZING ANTIBODY-LIKE MOLECULE
Applicant: Pharmacia & Upjohn Company
Published: 26 June 1997
- (11) International Patent Publication No. WO 97/17614
PEPTIDES WHICH ENHANCE TRANSPORT ACROSS TISSUES AND METHODS OF IDENTIFYING AND USING THE SAME
Applicant: Elan Corporation, PLC et al.
Published: 15 May 1997
- (12) European Patent Publication No. 0 773 441 A1
MOLECULES THAT HOME TO A SELECTED ORGAN OR TISSUE IN VIVO AND METHODS OF IDENTIFYING SAME
Applicant: La Jolla Cancer Research Foundation
Published: 14 May 1997
- (13) U.S. Patent No. 5,622,699 to Ruoslahti et al.
METHOD OF IDENTIFYING MOLECULES THAT HOME TO A SELECTED ORGAN IN VIVO
Issued: April 22, 1997
[Corresponds to EP 0 773 441 A1 cited above.]

In the International Preliminary Examination Report, the invention was found to possess novelty, inventive step and industrial applicability.

Applicants also provide copies of the following references discussed in the

Specification of the Application:

- (14) "Making Antibodies by Phage Display Technology",
Greg Winter et al., Annu. Rev. Immunol., Vol. 12 (1994)
pp. 433-455.
[Discussed at Page 20 of the Specification.]
- (15) "Combinatorial infection and in vivo recombination: a strategy for making large phage antibody repertoires", Peter Waterhouse et al.,
Nucleic Acids Research, Vol. 21, No. 9 (1993) pp. 2265-2266.
[Discussed at Page 20 of the Specification.]

- (16) "Isolation of high affinity human antibodies directly from large synthetic repertoires", Andrew D. Griffiths et al., The EMBO Journal, Vol. 13, No. 14 (1994) pp. 3245-3260.
[Discussed at Page 20 of the Specification.]
- (17) "An Antibody Fragment from a Phage Display Library Competes for Ligand Binding to the Low Density Lipoprotein Receptor Family and Inhibits Rhinovirus Infection", Regina A. Hodits et al., The Journal of Biological Chemistry, Vol. 270, No. 41 (October 13, 1995) pp. 24078-24085.
[Discussed at Page 20 of the Specification.]
- (18) "Phage antibodies: filamentous phage displaying antibody variable domains", John McCafferty et al., Nature, Vol. 348 (December 6, 1990) pp. 552-554.
[Discussed at Page 20 of the Specification.]
- (19) "Assembly of combinatorial antibody libraries on phage surfaces: The gene III site", Carlos F. Barbas, III et al., Proc. Natl. Acad. Sci. USA, Vol. 88 (September 1991) pp. 7978-7982.
[Discussed at Page 20 of the Specification.]
- (20) "Clonal Selection and Amplification of Phage Displayed Antibodies by Linking Antigen Recognition and Phage Replication", Marta Dueñas et al., Biotechnology, Vol. 12 (October 1994) pp. 999-1002.
[Discussed at Page 21 of the Specification.]
- (21) "Use of Living Columns to Select Specific Phage Antibodies", Andrew Bradbury et al., Biotechnology, Vol. 11 (December 1993) pp. 1565-1569.
[Discussed at Page 21 of the Specification.]
- (22) "Human Antibody Fragments Specific for Human Blood Group Antigens from a Phage Display Library", James D. Marks et al., Biotechnology, Vol. 11 (October 1993) pp. 1145-1149.
[Discussed at Page 21 of the Specification.]
- (23) "Rapid selection of cell subpopulation-specific human monoclonal antibodies from a synthetic phage antibody library", John De Kruif et al., Proc. Natl. Acad. Sci. USA, Vol. 92 (April 1995) pp. 3938-3942.
[Discussed at Page 21 of the Specification.]

- (24) "Generation and selection of monoclonal antibodies, single-chain F_v and antibody fusion phage specific for human melanoma-associated antigens", J.M. Kupsch et al., Melanoma Research, Vol. 5 (1995) pp. 403-411.
[Discussed at Page 21 of the Specification.]
- (25) "Anti-melanoma antibodies from melanoma patients immunized with genetically modified autologous tumor cells: Selection of specific antibodies from single-chain F_v fusion phage libraries", Xiaohong Cai et al., Proc. Natl. Acad. Sci. USA, Vol. 92 (July 1995) pp. 6537-6541.
[Discussed at Page 21 of the Specification.]
- (26) "Epithelial-to-mesenchymal change of differentiation. From embryogenetic mechanism to pathological patterns", M. Guarino, Histol Histopathol, Vol. 10 (1995) pp. 171-184.
[Discussed at Page 22 of the Specification.]
- (27) "Loss of the Tumorigenic Phenotype with *in Vitro*, but not *in Vivo*, Passaging of a Novel Series of Human Bronchial Epithelial Cell Lines: Possible Role of an $\alpha 5/\beta 1$ -Integrin-Fibronectin Interaction", Joan H. Schiller et al., Cancer Research, Vol. 55, (December 15, 1995) pp. 6215-6221.
[Discussed at Page 22 of the Specification.]
- (28) "*In vitro* and *in vivo* regulation of human tumor antigen expression by human recombinant interferons: a review", F. Guadagni et al., The International Journal of Biological Markers, Vol. 9, No. 1 (1994) pp. 53-60.
[Discussed at Page 22 of the Specification.]
- (29) "Engineering Subtilisin BPN' for Site-Specific Proteolysis", Paul Carter et al., PROTEINS: Structure, Function and Genetics, Vol. 6 (1989) pp. 240-248.
[Discussed at Page 22 of the Specification.]
- (30) "Neutralizing Recombinant Human Antibodies to a Conformational V2- and CD4-Binding Site-Sensitive Epitope of HIV-1 gp120 Isolated by Using an Epitope-Masking Procedure", Henrik J. Ditzel et al., The Journal of Immunology, Vol. 154 (1995) pp. 893-906.
[Discussed at Page 22 of the Specification.]

- (31) "Brief Communication: Melanoma-Specific Antibodies Produced in Monkeys by Immunization with Human Melanoma Cell Lines", Richard S. Metzgar et al., J. Natl Cancer Inst, Vol. 50 (1973) pp. 1065-1068.
[Discussed at Page 22 of the Specification.]
- (32) "Spectrum of Melanoma Antigens on Cultured Human Malignant Melanoma Cells as Detected by Monkey Antibodies", Shuen-Kuei Liao et al., Cancer Research, Vol. 39 (January 1979) pp. 183-192.
[Discussed at Page 22 of the Specification.]
- (33) "Murine monoclonal anti-idiotope antibody breaks unresponsiveness and induces a specific antibody response to human melanoma-associated proteoglycan antigen in cynomolgus monkeys", Panchanon Chattopadhyay et al., Prac. Natl. Acad. Sci. USA, Vol. 89 (April 1992) pp. 2684-2688.
[Discussed at Page 23 of the Specification.]
- (34) "Human neoplasms elicit multiple specific immune responses in the autologous host", Ugur Sahin et al., Prac. Natl. Acad. Sci. USA, Vol. 92 (December 1995) pp. 11810-11813.
[Discussed at Page 23 of the Specification.]
- (35) "Human Antibodies with Sub-nanomolar Affinities Isolated from a Large Non-immunized Phage Display Library", Tristan J. Vaughan et al., Nature Biotechnology, Vol. 14 (March 1996) pp. 309-314.
[Discussed at Page 23 of the Specification.]
- (36) "Monoclonal antibody--superantigen fusion proteins: Tumor-specific agents for T-cell-based tumor therapy", Mikael Dohlsten et al., Prac. Natl. Acad. Sci. USA, Vol. 91 (September 1994) pp. 8945-8949.
[Discussed at Page 23 of the Specification.]
- (37) "Three-dimensional Structure of an Antigen-Antibody Complex at 2.8 Å Resolution", A. G. Amit et al., Science, Vol. 233 (August 1986) pp. 747-753.
[Discussed at Page 23 of the Specification.]

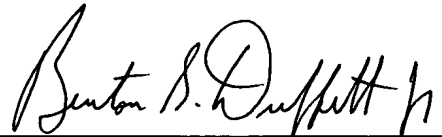
- (38) "Filamentous Fusion Phage: Novel Expression Vectors That Display Cloned Antigens on the Virion Surface", George P. Smith, Science, Vol. 228 (June 14, 1985) pp. 1315-1317.
[Discussed at Page 23 of the Specification.]
- (39) "Culture Medium for Enterobacteria", Frederik C. Neidhardt et al., Journal of Bacteriology, Vol. 119, No. 3 (September 1974) pp. 736-747.
[Discussed at Page 24 of the Specification.]
- (40) "Characterization of two distinct MHC class II binding sites in the superantigen staphylococcal enterotoxin A", Lars Abrahmsén et al., The EMBO Journal, Vol. 14, No. 13 (1995) pp. 2978-2986.
[Discussed at Page 24 of the Specification.]

The documents are being submitted within three (3) months of the filing or entry of the national stage of this application or before the first Office Action on the merits, whichever is later, therefore no fee or certification is required under 37 C.F.R. §1.97(b).

To assist the Examiner, the documents are listed on the attached form PTO-1449. The examination and allowance of this Application are respectfully requested.

Respectfully submitted,

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